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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/573,163	02/28/2007	Guido Bold	33381-US-PCT	6615

1095 7590 07/24/2009

NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
THOMAS, TIMOTHY P	

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
07/24/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/573,163	BOLD ET AL.	
	Examiner	Art Unit	
	TIMOTHY P. THOMAS	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *1-9 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-18* is/are rejected.

7)☒ Claim(s) *10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/23/2006; 5/18/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, claims 10-18 in the reply filed on 12/17/2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Applicant's election of 1-(4-chloroanilino)-4-(4-pyridylmethyl)phthalazine (PTK787) as the single VEGF inhibitor and the histone deacylase inhibitor, N-hydroxy-3-[4-[[[2-(2-methyl-1H-indol-3-yl)-ethyl]-amino]methyl]phenyl]-2E-2-propeneamide (LBH589) as the other chemotherapeutic agent, with the identification that claims 10-18 read on the elected invention, in the replies filed on 12/17/2008 and 5/7/2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Claims 1-9 and 19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without specifying traverse in the reply filed on 12/17/2008.

Claim Objections

4. Claim 10 is objected to because of the following informalities: the claim has periods after each of the items i.-xxvii., listed under (b). As pointed out in MPEP 608.01(m), each claim is to begin with a capital letter and end with a period. Periods

may not be used elsewhere in the claims except for abbreviations. Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 10-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Regarding claims 10-12, the phrases "for example" (e.g.) and “preferably” recited in claim 10 render the claim and claims 11-12, dependent from claim 10, indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

8. Regarding claims 10-16, the abbreviations VEGF and HDAC, without the meaning accompanying the abbreviation at the first occurrence in the claims does not make clear that the meaning recited in the specification controls the meaning of the abbreviations in the claims.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 10-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wood et al. ("PTK787/ZK 222584, a Novel and Potent Inhibitor of Vascular Endothelial Growth Factor Receptor Tyrosine Kinases, Impairs Vascular Endothelial Growth Factor-induced Responses and Tumor Growth after Oral Administration"; 2000; Cancer Research; 60: 2178-2189) and Remiszewski et al. (US 6,552,065 B2; 2003 Apr; filed 2001; priority 2000).

Wood teaches the succinate salt of the elected compound PTK787 (title, abstract); that the compound is a potent inhibitor of vascular endothelial growth factor

(VEGF) receptor tyrosine kinases, active in the submicromolar range, and inhibits other class III kinases, such as PDGF receptor β tyrosine kinase, c-Kit and c-Fms, but at higher concentrations (abstract); the compound inhibits the growth of several human carcinomas grown in mice and a murine renal carcinoma, inhibition of microvessel formation is present in the interior of the tumor (abstract); the compound is well tolerated, does not impair wound healing, and does not have any significant effects on circulating blood cells or bone marrow leukocytes as a single agent or impair hematopoetic recovery after concomitant cytotoxic anti-cancer agent challenge (abstract); the novel compound has therapeutic potential for the treatment of solid tumors and other diseases where angiogenesis plays an important role (abstract); various therapies are mentioned, which include cyclic therapy in combination with conventional antitumor thrapies, for treatment of cancer (p. 2187, right, top paragraph); the compound is a potent, p.o. active, and well tolerated inhibitor of VEGF-mediated responses, this excellent oral activity and tolerability of this compound favor its use for prolonged treatment, including for cancers dependent on VEGF for their vascularization (p. 2187, last paragraph). Wood does not teach PTK787 in combination with the specific elected HDAC inhibitor compound, LBH589.

Remiszewski teaches hydroxamate compounds which are deacetylase inhibitors, compounds which are suitable for pharmaceutical compositions having anti-proliferative properties (abstract); the elected other chemotherapeutic agent, the histone deacylase inhibitor, N-hydroxy-3-[4-[[[2-(2-methyl-1H-indol-3-yl)-ethyl]-amino]methyl]phenyl]-2E-2-propeneamide (LBH589) is taught as an important compound of formula Ie (col. 12,

lines 24-27); the compounds are useful for treating proliferative diseases, including a variety of cancer types and metastases (col. 22, lines 11-29).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine PTK787 with LBH589 into a single composition, giving the elected pharmaceutical composition of the instant claims. The motivation would have been the combination of two different art-recognized anticancer agents with two complementary mechanisms of action.

As pointed out in MPEP 2144.06 (I), "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose…. [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Conclusion

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIMOTHY P. THOMAS whose telephone number is (571)272-8994. The examiner can normally be reached on Monday-Thursday 6:30 a.m. - 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Timothy P Thomas/
Examiner, Art Unit 1614